

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1. (Currently amended) A screening method comprising:

(a) providing a first plurality of bacterial host cells secreting a first Fd of an antibody that binds to a first antigen, wherein the first plurality of bacterial host cells contains DNA encoding the first Fd linked to a bacterial secretion signal peptide;

(b) introducing an antibody light chain ~~fragment~~-phage library encoding a plurality of different light chains, each linked to a bacterial secretion signal and a phage membrane anchor domain, into the first plurality of host cells to cause secretion of phage libraries presenting two-chain antibody fragments, each antibody fragment comprising the first Fd and a light chain ~~fragment~~;

(c) selecting a phage library that displays antibody fragments that bind specifically to the first antigen;

(d) introducing the phage library selected in step (c) into a second plurality of bacterial host cells secreting a second Fd that is the Fd of an antibody that binds to a second antigen different from the first antigen, to create phage libraries presenting two-chain antibody fragments, each comprising the second Fd and a light chain ~~fragment~~, wherein the second plurality of bacterial host cells contains DNA encoding the second Fd linked to a bacterial secretion signal peptide; and

(e) selecting, from the phage libraries created in step (d), a phage library that displays two-chain antibody fragments that bind specifically to the second antigen.

2. (Currently amended) A screening method comprising:

(a) providing a first plurality of bacterial host cells secreting a first Fd of an antibody that binds to a first antigen, wherein the first plurality of bacterial host cells contains DNA encoding the first Fd linked to a bacterial secretion signal;

(b) introducing an antibody light chain-~~fragment~~ phage library encoding a plurality of different light chains, each linked to a bacterial secretion signal and a phage membrane anchor domain, into the first plurality of host cells to cause secretion of phage libraries presenting two-chain antibody fragments, each antibody fragment comprising the first Fd and a light chain ~~fragment~~;

(c) selecting a phage library that displays antibody fragments that bind specifically to the first antigen;

(d) introducing the phage library selected in step (c) into a second plurality of bacterial host cells secreting a second Fd comprising an amino acid sequence different from that of the first Fd, to create phage libraries displaying two-chain antibody fragments, each antibody fragment comprising the second Fd and a light chain, wherein the second plurality of bacterial host cells contains DNA encoding the second Fd linked to a bacterial secretion signal; and

(e) selecting, from the phage libraries created in step (d), a phage library that displays antibodiesantibody fragments that bind specifically to an antigen recognized by the second Fd.

3. (Canceled)

4. (Previously Presented) The method of claim 1, wherein the host is *E. coli*.

5. (Previously presented) The method of claim 1, wherein steps (b) to (e) are carried out twice or more, with each subsequent round beginning with the phage library selected in step (e) of the prior round.

6. (Currently amended) The method of claim 1, wherein the method further comprises the steps of:

(f) introducing the phage library selected in step (e) into a third plurality of bacterial host cells secreting a third Fd that is the Fd of an antibody that binds to a third ~~desired~~-antigen different from the first and second antigens of steps (a) and (d), to create phage libraries that display two-chain antibody fragments comprising the third Fd and a light chain-~~fragment~~, wherein the third plurality of bacterial host cells contains DNA encoding the third Fd linked to a bacterial secretion signal; and

(g) selecting a phage library that displays two-chain antibody fragments that bind specifically to the third ~~desired~~-antigen.

7. (Currently amended) The method of claim 2, wherein the method further comprises the steps of:

(f) introducing the phage library selected in step (e) into a third plurality of bacterial host cells secreting a third Fd comprising an amino acid sequence different from those of the first and second Fd's, to cause secretion of phage libraries that display two-chain ~~antibodies~~antibody fragments, each being composed of the third Fd and a light chain-~~fragment~~, wherein the third plurality of bacterial host cells contains DNA encoding the third Fd linked to a bacterial secretion signal; and

(g) selecting a phage library that displays antibody fragments that bind specifically to an antigen recognized by the third Fd.

8-9. (Cancelled)

10. (Withdrawn) A method for generating antibody light chains, wherein the method comprises the steps of:

(a) selecting an antibody light chain from the screening method of claim 1;

(b) generating a vector capable of expressing the selected light chain based on its genetic sequence;

(c) introducing the vector into a host cell; and

(d) culturing said host cell.

11-13. (Cancelled)

14. (Previously presented) The method of claim 2, wherein the host is *E. coli*.

15. (Previously presented) The method of claim 2, wherein steps (b) to (e) are carried out twice or more, with each subsequent round beginning with the phage library selected in step (e) of the prior round.

16-17. (Cancelled)

18. (Withdrawn) A method for generating antibody light chains, wherein the method comprises the steps of:

- (a) selecting an antibody light chain from the screening method of claim 2;
- (b) generating a vector capable of expressing the selected light chain based on its genetic sequence;
- (c) introducing the vector into a host cell; and
- (d) culturing said host cell.

19-26. (Canceled)

27. (Currently amended) A method of producing a multi-specific antibody fragment, the method comprising

- (i) carrying out the screening method of claim 1 to select a phage library that displays two-chain antibody fragments that bind specifically to the second antigen;

(ii) selecting from the phage library of (i) a phage displaying a two-chain antibody fragment that binds to the second antigen and comprises the second Fd and a light chain fragment (the "selected light chain-fragment");

(iii) producing a host cell comprising nucleic acid encoding (A) a light chain comprising the sequence of the selected light chain-fragment, (B) a heavy chain comprising the sequence of the first Fd, and (C) a heavy chain comprising the sequence of the second Fd;

(iv) culturing the host cell of (iii) so that it expresses (A), (B), and (C) and assembles (A), (B) and (C) into a multispecific antibody comprising a copy of (B), a copy of (C), and two copies of (A), wherein (A) serves as a common light chain-fragment for both (B) and (C).

28. (Currently amended) A method of producing a multi-specific antibody fragment, the method comprising

(i) carrying out the screening method of claim 2 to select a phage library that displays two-chain antibody fragments that bind specifically to the antigen recognized by the second Fd;

(ii) selecting from the phage library of (i) a phage displaying a two-chain antibody fragment that binds to the antigen recognized by the second Fd and comprises the second Fd and a light chain-fragment (the "selected light chain-fragment");

(iii) producing a host cell comprising nucleic acid encoding (A) a light chain comprising the sequence of the selected light chain-fragment, (B) a heavy chain comprising the sequence of the first Fd, and (C) a heavy chain comprising the sequence of the second Fd;

(iv) culturing the host cell of (iii) so that it expresses (A), (B), and (C) and assembles (A), (B) and (C) into a multispecific antibody comprising a copy of (B), a copy of (C), and two copies of (A), wherein (A) serves as a common light chain-fragment for both (B) and (C).

29. (Previously presented) The method of claim 27, wherein the host is *E. coli*.

30. (Previously presented) The method of claim 28, wherein the host is *E. coli*.

31. (Currently amended) A method of producing a multi-specific antibody fragment, the method comprising

- (i) carrying out the screening method of claim 5 to ultimately select a phage library that displays two-chain antibody fragments that bind specifically to the second antigen;
- (ii) selecting from the phage library of (i) a phage displaying a two-chain antibody fragment that binds to the second antigen and comprises the second Fd and a light chain fragment (the "selected light chain-fragment");
- (iii) producing a host cell comprising nucleic acid encoding (A) a light chain comprising the sequence of the selected light chain-fragment, (B) a heavy chain comprising the sequence of the first Fd, and (C) a heavy chain comprising the sequence of the second Fd;
- (iv) culturing the host cell of (iii) so that it expresses (A), (B), and (C) and assembles (A), (B) and (C) into a multispecific antibody comprising a copy of (B), a copy of (C), and two copies of (A), wherein (A) serves as a common light chain-fragment for both (B) and (C).

32. (Currently amended) A method of producing a multi-specific antibody fragment, the method comprising

- (i) carrying out the screening method of claim 7 to ultimately select a phage library that displays two-chain antibody fragments that bind specifically to the antigen recognized by the third Fd;
- (ii) selecting from the phage library of (i) a phage displaying a two-chain antibody fragment that binds to the antigen recognized by the third Fd and comprises the third Fd and a light chain-fragment (the "selected light chain-fragment");
- (iii) producing a host cell comprising nucleic acid encoding (A) a light chain comprising the sequence of the selected light chain-fragment, (B) a heavy chain comprising the sequence of the first Fd, (C) a heavy chain comprising the sequence of the second Fd, and (D) a heavy chain comprising the sequence of the third Fd;
- (iv) culturing the host cell of (iii) so that it expresses (A), (B), (C), and (D) and assembles (A), (B), (C), and (D) into a multispecific antibody comprising a copy of (B), a copy

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Serial No. : 10/542,839
Filed : December 13, 2005
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Attorney's Docket No.: 14875-0148US1 / C1-A0231P-US

of (C), a copy of (D), and three copies of (A), wherein (A) serves as a common light chain fragment for all of (B), (C), and (D).